7 What Is the Role of Noninvasive Ventilation in the Intensive Care Unit?

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Noninvasive ventilation (NIV) has assumed an important role in the intensive care unit (ICU), with increasing use during the past 15 years. It is now considered the ventilatory mode of first choice for such forms of acute respiratory failure (Table 7-1). Multiple randomized controlled trials have demonstrated that NIV improves outcomes in these forms of respiratory failure. Improved outcomes include avoidance of intubation and reduced morbidity and mortality compared with conventional therapy including intubation. In addition, the role of NIV is expanding as more studies are completed in other forms of respiratory failure. There are encouraging results from trials evaluating NIV use in postoperative respiratory failure and preoxygenation of patients with hypoxemic respiratory failure before intubation in the ICU. The results are less clear in other forms of respiratory failure such as severe asthma, pneumonia, and acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) as well as in postextubation respiratory failure in patients with non–chronic obstructive pulmonary disease (COPD).

SELECTING PATIENTS FOR NONINVASIVE VENTILATION

The first question that should be addressed when selecting patients for NIV is whether the patient needs ventilatory support. Such patients usually have moderate to severe respiratory distress, signs of increased work of breathing such as tachypnea, increased use of accessory muscles, or abdominal paradox. Arterial blood gases should be obtained before starting NIV to assess the severity of the gas exchange derangement (particularly partial pressure of arterial carbon dioxide [$Paco_2$]) and to establish a baseline for comparison after the first 1 to 2 hours. Acutely ill patients should be monitored initially in an ICU or step-down unit to ensure that the patient is improving and tolerating the mask. Trials have shown that the response at the 1- to 2-hour time point is highly predictive of subsequent outcome; patients improving at this point are likely to succeed, but those failing to respond are likely to fail. Risk factors for failure after 2 hours of NIV are listed in Table 7-2.[1-3]

CONTRAINDICATIONS TO NONINVASIVE VENTILATION

When the need for ventilatory assistance is established, candidates for NIV should be screened for possible contraindications. NIV is contraindicated in patients with cardiopulmonary arrest because there is no time to place a mask and make adjustments. Any patient in shock requiring more than low doses of vasopressors is not a good candidate,[4] nor is the patient with a large acute myocardial infarction, uncontrolled arrhythmias or cardiac ischemia, or a large upper gastrointestinal bleed that is threatening the upper airway. Uncooperative and agitated patients and those with severe claustrophobia are unlikely to tolerate the mask. Patients with copious secretions, impaired swallowing, and frequent vomiting are at risk for aspiration and are poor candidates. Recent upper gastrointestinal surgery is also a relative contraindication because of the risk for abdominal distension and suture line rupture, although there have been some reports of successful use of NIV in these patients. Upper airway obstruction due to epiglottitis or angioedema is best treated with intubation to avoid progression to complete airway obstruction and the need for emergent cricothyrotomy, although upper airway obstruction due to glottic edema after extubation may respond well.[5] Impaired mental status is a relative contraindication, with one of the major concerns being the patient's inability to remove the mask in the event of vomiting. However, hypercapnic coma in patients with COPD exacerbations should not be considered a contraindication, and one trial has shown good outcomes with NIV use in these patients[6] (Table 7-3).

APPLICATIONS OF NONINVASIVE VENTILATION IN THE INTENSIVE CARE UNIT

NIV has been tried for many types of respiratory failure in the ICU. However, the evidence to support these applications varies depending on the diagnosis or circumstance. Table 7-4 lists the most common applications and the levels of evidence supporting them. In the following, we discuss the

Table 7-1 Indications for NIV in Critically Ill Patients

- Exacerbations of COPD
- Acute cardiogenic pulmonary edema
- Hypoxemic respiratory failure in immunocompromised patients
- Facilitating extubation in patients with COPD who fail spontaneous breathing trials

COPD, chronic obstructive pulmonary disease; *NIV*, noninvasive ventilation.

Table 7-2 Risk Factors for Failure of NIV

- pH < 7.25
- Relative risk >35
- APACHE II score >29
- ALI/ARDS
- Pneumonia
- Severe hypoxemia
- Shock
- Metabolic acidosis
- Impaired mental status

ALI, acute lung injury; *APACHE*, Acute Physiology and Chronic Health Evaluation; *ARDS*, acute respiratory distress syndrome; *NIV*, noninvasive ventilation.

Table 7-3 Contraindications to NIV

- Cardiopulmonary arrest, shock
- Uncontrolled cardiac ischemia or arrhythmias
- Uncooperative or agitated
- Severe upper gastrointestinal hemorrhage
- Coma, nonhypercapnic
- High aspiration risk, vomiting
- Copious secretions
- Upper airway obstruction
- Severe bulbar dysfunction
- Recent esophageal or upper airway surgery
- Multiorgan dysfunction
- Inability to fit mask because of craniofacial abnormalities

NIV, noninvasive ventilation.

evidence supporting the various applications in more detail, starting with those supported by the strongest evidence.

First-Line Therapy

COPD Exacerbations

Multiple randomized, trials meta-analyses, and, more recently, comparative effectiveness analyses have shown decreased intubation and improved mortality rates with NIV use compared with standard medical therapy in patients with exacerbations of COPD.[7-13] Therefore NIV should be considered the standard of care in patients with COPD exacerbations requiring ventilatory support in the absence of contraindications. The physiologic rationale in these patients is that NIV unloads the inspiratory muscles and increases tidal volume, decreases the dead space-to-tidal volume ratio, lowers respiratory rate, and improves alveolar ventilation.[7] The addition of positive end-expiratory pressure (PEEP) decreases the work of breathing by decreasing the inspiratory threshold load imposed by auto-PEEP that is frequently present in these patients.[14]

Table 7-4 Indications for NIV Use

Strength of Recommendation*	Indication for NIV	Quality of Evidence†
Strong	COPD exacerbations	A
	Acute cardiogenic pulmonary edema	A
	Immunocompromised states	A
	Facilitating extubation in COPD	A
Intermediate	Postoperative respiratory failure	B
	Preoxygenation in hypoxemic respiratory failure	B
	Facilitation of flexible bronchoscopy	B
	Palliation in DNR/DNI patients	B
	Postextubation respiratory failure	B
Weak	ALI/ARDS	C
	Neuromuscular disease	C
	Pneumonia	C
	Status asthmaticus	C

*Strength of recommendation: strong, recommended therapy; intermediate, strongly consider in good candidates for NIV; weak, cautious trial can be performed in otherwise excellent candidates for NIV.

†Quality of evidence: *A*, multiple randomized controlled trials showing benefit with NIV; *B*, single randomized trial or nonrandomized trials showing benefit with NIV; *C*, conflicting evidence or evidence of harm with NIV.

ALI, acute lung injury; *ARDS*, acute respiratory distress syndrome; *COPD*, chronic obstructive pulmonary disease; *DNI*, do not intubate; *DNR*, do not resuscitate; *NIV*, noninvasive ventilation.

Acute Cardiogenic Pulmonary Edema

Multiple randomized trials and meta-analyses have shown that either continuous positive airway pressure (CPAP) alone or NIV lowers intubation rates and mortality when compared with conventional medical therapy in patients with cardiogenic pulmonary edema.[15-25] The benefit in these patients primarily reflects an increase in intrathoracic pressure. Higher intrathoracic pressure increases functional residual capacity (FRC), recruiting flooded alveoli, improving gas exchange, and improving lung compliance. An increase in intrathoracic pressure also reduces cardiac preload and afterload, improving

hemodynamics in most patients with cardiogenic pulmonary edema.[26,27] Longer term use of CPAP in stable congestive heart failure patients improved left ventricular ejection fraction, decreased mitral regurgitation, and decreased atrial natriuretic peptide levels compared with controls.[28] Whether CPAP alone or NIV (i.e., pressure support plus PEEP) is the preferred modality is unclear. An early study showed an increased rate of myocardial infarctions with NIV,[24] but subsequent trials and meta-analyses have failed to replicate this and have instead demonstrated that both modalities similarly reduce the need for intubation and lower mortality rates.[17,25] Although CPAP has been suggested as the preferred initial modality because of its greater simplicity and lower expense, most centers initially use NIV because bilevel devices are readily available and unloading of the inspiratory muscles may be achieved more quickly. In unstable patients with pulmonary edema complicating ST-elevation myocardial infarction, or in the presence of cardiogenic shock, early intubation is recommended.

Immunocompromised States

NIV decreases mortality compared with oxygen therapy alone in immunocompromised patients with hypoxemic respiratory failure. This includes patients with hematologic malignancies, patients who have had solid organ transplantation, or patients with HIV or AIDS.[29,30] The beneficial effects are attributed to the avoidance of infectious complications related to intubation. These patients are particularly vulnerable to intubation-associated pneumonias and septic complications.[31] We would recommend instituting this therapy early when there is a window of opportunity to avoid the progression to overt respiratory failure and the need for intubation. Once intubated, mortality rates among the immunocompromised may be very high,[31] although they appear to be declining.[32] In a retrospective observational study of patients with malignancy (including hematologic malignancies) and ARDS, mortality rates improved over time (89% in the first 5 years compared with 52% over the last 5 years). However, there was continued evidence of high mortality (68.5%) in patients with severe ARDS (partial pressure of arterial oxygen (Pao_2)/fraction of inspired oxygen (Fio_2) ≤ 100). Higher rates of NIV failure were observed in patients with moderate or severe ARDS and in patients experiencing NIV failure.[32]

Extubating Patients with COPD

Studies have shown decreased duration of mechanical ventilation and improved mortality when intubated COPD patients who have failed spontaneous breathing trials are extubated and supported with NIV.[33,34] However, this approach should be used with extreme caution. Patients should be excellent candidates for NIV in every other way—hemodynamically stable, cooperative, having a good cough and manageable secretions, and able to be ventilated with pressure support levels not exceeding 15 cm H_2O. Furthermore, initial intubation should not have been technically difficult because of the potential for catastrophe should these patients require emergent reintubation. The authors have found early extubation to NIV to be useful in avoiding the need for tracheostomies in such patients. However, if this approach fails and reintubation is necessary, we usually proceed to prompt placement of a surgical airway.

OTHER INTENSIVE CARE UNIT APPLICATIONS

Preoxygenation Before Intubation

NIV can be an effective way of preoxygenating critically ill patients with hypoxemic respiratory failure before intubation.[35] In one randomized trial,[35] patients managed with NIV in preparation for intubation had improved oxygen saturations and a decreased incidence of significant desaturations during intubation. Anecdotally, we have had good success using this technique in our ICU. The beneficial effect of NIV likely is due to an increase in FRC with increased oxygen stores.

Flexible Bronchoscopy

NIV has been used during flexible bronchoscopy to avoid intubation.[36,37] This technique may be especially useful in immunocompromised patients at high risk for infectious complications from airway invasion. The technique involves passing the bronchoscope through an adapter attached to the NIV mask. In one trial, flexible bronchoscopy performed in eight immunocompromised patients with hypoxemic respiratory failure improved oxygenation compared with oxygen supplementation alone. None of these patients required intubation.[37] Because of the risk for respiratory deterioration during the procedure, clinicians should be prepared for possible emergency intubation. An alternative technique to consider in these patients is performing bronchoscopy through a supraglottic device, such as a laryngeal mask airway, but this technique requires deep sedation.

Postoperative Respiratory Failure

One randomized trial in patients with postoperative respiratory failure after lung resection surgery showed decreased intubation rates and mortality with NIV compared with standard therapy.[38] Another randomized trial found that prophylactic CPAP at 10 cm H_2O for 12 to 24 hours after thoracoabdominal aortic surgery reduced pulmonary complications and decreased hospital length of stay compared with oxygen supplementation alone.[39] Twenty-four hours of CPAP use after upper abdominal surgery was also associated with fewer intubations, a decreased occurrence of pneumonia and septic complications, and shorter ICU lengths of stay than oxygen therapy alone.[40] Similar efficacy has been reported for postgastric bypass patients.[41] One of the main reasons for the beneficial effect of CPAP or NIV in the postoperative setting is the avoidance of a sedation- or analgesic-associated reduction in the FRC and concomitant impairment of cough. These predispose to atelectasis, hypoxemia, pneumonia, and respiratory failure.

Obesity Hypoventilation Syndrome

Acute hypercapnic respiratory failure related to obesity hypoventilation is becoming more prevalent given the

obesity epidemic in the general population. A single-center prospective observational study examined the use of NIV in these patients. Compared with COPD patients with acute hypercapnic respiratory failure, patients with obesity hypoventilation syndrome (OHS) were slightly older, more often female, and had similar initial arterial blood gas values. These patients also had lower late NIV failure and hospital mortality rates and better survivals at 1 year. The authors concluded that when used for acute hypercapnic respiratory failure in the ICU, NIV for OHS patients has similar efficacy and better outcomes than for COPD patients.[42]

Neuromuscular Disease

Evidence supports the use of home NIV in patients with neuromuscular disorders such as myopathies, muscular dystrophies, spinal muscular atrophy, scoliosis, and amyotrophic lateral sclerosis.[43-46] NIV reverses hypoventilation, stabilizes the upper airway, and improves obstructive sleep apnea. When these patients are admitted to the hospital, it is usually because of a respiratory infection. Aggressive management of secretion retention is paramount in avoiding respiratory catastrophe. Such patients should be managed only in an ICU where they can be monitored closely and frequently assisted with coughing. They should receive around-the-clock NIV and help with coughing using manually assisted coughing combined with mechanical insufflation and exsufflation ("cough assist") as often as necessary.[47] There is a subset of rapidly progressive neuromuscular disorders, including myasthenic crisis and Guillain-Barré syndrome, that involves "bulbar" muscles, impairing swallowing and the ability to mobilize secretions. Patients with these usually require preemptive intubation to avoid an unanticipated respiratory arrest, although a retrospective observational study[48] in patients with myasthenic crises showed that early use of NIV reduced the need for intubation and prolonged mechanical ventilation.

Palliative Care

NIV has a potential role in the treatment of patients with do-not-resuscitate/do-not-intubate (DNR/DNI) orders and end-of-life care. A study of NIV use in patients with heterogeneous respiratory failure and DNR/DNI status showed favorable outcomes in those with the types of respiratory failure expected to do well with NIV, such as COPD and cardiogenic pulmonary edema.[49] NIV can also be used for palliation of dyspnea or to extend life for a few hours to permit settling of affairs, but it should be discontinued if the mask is poorly tolerated or if dyspnea is not improved.

POSSIBLE ROLE IN THE INTENSIVE CARE UNIT

Asthma

Evidence regarding the use of NIV in severe asthma is lacking. One randomized trial in an Israeli emergency department of patients with acute asthma showed that NIV improved forced expiratory volume in 1 second more rapidly and decreased the need for hospitalization compared with sham NIV.[50] However, the patients were not in respiratory failure, and all patients had normal arterial blood gases. A Cochrane review concluded that more trials are needed before NIV can be recommended in this setting.[51] NIV can be tried cautiously in patients with asthma who fail to respond to initial bronchodilator therapy and have persistently increased work of breathing. This approach can be combined with helium-oxygen mixtures and continuous nebulization, although evidence to support this combination of therapies is lacking. However, patients with acute asthma treated with NIV must be watched closely because they can rapidly deteriorate. Emergency intubation can be dangerous if delayed too long because these patients can have profound oxygen desaturations and can also progress to hemodynamic collapse from hyperinflation and increased intrathoracic pressure.

Pneumonia

Acute pneumonia has long been considered a risk factor for NIV failure.[3] A trial evaluating NIV use in heterogeneous respiratory failure showed very poor outcome in the group of patients with pneumonia, with all such patients requiring intubation.[52] Another study evaluated NIV use in patients with hypoxemic respiratory failure and identified community-acquired pneumonia as a subcategory with a high NIV failure rate (50% intubation rate).[3] A randomized trial showed benefit of NIV in patients with severe community-acquired pneumonia but only in the subgroup with underlying COPD.[2] These data suggest that NIV should not be used routinely in patients with severe pneumonia.

Acute Lung Injury and Acute Respiratory Distress Syndrome

Similar to pneumonia, the evidence does not support the routine use of NIV in patients with ALI/ARDS. In a trial by Antonelli et al.,[3] ARDS, along with a higher Simplified Acute Physiology (SAPS) II score (>35), was identified as a risk factor for NIV failure. A recent trial evaluated NIV use in patients with ALI/ARDS and found a very high rate of failure (70%). Risk factors for NIV failure included shock (100% intubation rate), metabolic acidosis, and severe hypoxemia. The authors concluded that NIV should be used cautiously, if at all, if risk factors for failure are present.[1] A recent cohort study showed that some patients with ARDS may benefit from NIV. When used as first-line therapy for ARDS patients who are not yet undergoing intubation on admission to the ICU, NIV was able to prevent subsequent intubation in 54% of patients. A SAPS II score higher than 34 and lack of improvement in Pao_2/Fio_2 ratio to more than 175 after 1 hour of therapy were risk factors for NIV failure.[53] This latest study suggests that some patients with ALI/ARDS, especially less severely ill patients without shock, metabolic acidosis, or severe hypoxemia, may benefit from NIV. Close monitoring is essential, and if the Pao_2/Fio_2 ratio does not improve after 1 hour, then intubation and mechanical ventilation should be initiated.

Interstitial Lung Disease

ICU admissions for acute respiratory failure due to interstitial lung disease are associated with a high mortality rate. However, in selected patients, NIV may play a role in preventing intubation and improving survival. A prospective observational study[54] revealed that patients with Acute Physiology and Chronic Health Evaluation (APACHE) II scores less than 20 and mixed interstitial lung disease requiring noncontinuous NIV had a higher survival rate than those requiring continuous NIV or invasive mechanic ventilation. Likewise, a small retrospective study[55] of patients who had idiopathic pulmonary fibrosis with acute respiratory failure found a poor overall prognosis; however, for those who survived, NIV use was associated with a shorter ICU length of stay and improved 90-day survival. Interestingly, patients in this study with a higher level of the N-terminal prohormone brain natriuretic peptide (NT-proBNP) at baseline had a higher risk of NIV failure.

Postextubation Respiratory Failure

A large multicenter trial evaluated a heterogeneous group of patients with postextubation respiratory failure and randomized patients to treatment with NIV or standard therapy. Unexpectedly, the group that received NIV had an increased ICU mortality, as well as a 10-hour longer delay before reintubation.[56] These results underscore the importance of proper patient selection, with certain causes such as pneumonia and ALI/ARDS having poor outcomes. It is also clear that not delaying a needed intubation is essential. Postextubation respiratory failure can be treated with NIV if the patient is without contraindications and has a form of respiratory failure likely to respond to NIV, such as COPD or cardiogenic pulmonary edema. Again, closely evaluating the patient at the 1- to 2-hour point is critical to avoid delaying intubation.

In addition, the results of studies evaluating prophylactic NIV use after extubation to avoid reintubation have been mixed. Several meta-analyses have revealed a potential benefit to immediate NIV application postextubation.[59,60] However, most patients enrolled in these studies underwent intubation because of acute respiratory failure from COPD, in which the benefit of NIV is well established (see previously). A randomized controlled study evaluating NIV use after planned extubation in a mixed group of patients found no difference in reintubation rates between early NIV and standard medical treatment.[61] However, a further, smaller, randomized controlled trial in patients with varied causes for their acute respiratory failure did show a reduced reintubation rate benefit when NIV was used immediately after extubation.[62] Further study is clearly needed on the use of NIV after extubation.

CONCLUSION

The role of NIV in the ICU is gaining importance as the evidence supporting its use in certain forms of acute respiratory failure accumulates. Some studies support the use of NIV to preoxygenate patients with hypoxemic respiratory failure before intubation, as well as to facilitate flexible bronchoscopy in certain patients at high risk for infectious or bleeding complications from endotracheal intubation. The results of NIV or CPAP use in postoperative respiratory failure are encouraging, and this application requires further study. Data to support use in other forms of respiratory failure, including severe pneumonia, status asthmaticus, ALI/ARDS, and hypoxemic respiratory failure after extubation, are weaker, but selected patients with these conditions can be tried on NIV as long as they are closely monitored and undergo intubation promptly if they fail to improve. Recent surveys have shown that the use of NIV is increasing in critical care units throughout Europe[63] and presumably also in the United States. Patients who undergo NIV should be monitored closely in an ICU or step-down unit for mask tolerance and leaks, respiratory rate, use of accessory muscles, synchrony with the ventilator, and gas exchange. A careful assessment within 1 to 2 hours is important in determining the likelihood of success with NIV and is usually sufficient to decide to continue NIV or intubation and initiate invasive mechanic ventilation. Future studies should further define the role of NIV in the ICU and will likely expand the use of this important technology.

AUTHORS' RECOMMENDATIONS

- NIV has become an important part of the critical care ventilator armamentarium.
- Strong evidence supports the use of NIV for acute respiratory failure associated with COPD exacerbations, acute cardiogenic pulmonary edema, and immunocompromised states.
- If used, NIV should be applied with caution and in a closely monitored setting for patients with OHS, asthma, pneumonia, or ARDS.
- Patients must be carefully selected for NIV, which should be reserved for patients who require ventilatory assistance but have no contraindications.
- If patients are not improving within the first 1 or 2 hours of NIV, then intubation should be performed without further delay.

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